The crucial role of the GLG on AMR to support antibacterial innovation

Kevin Outterson, Executive Director
Austin B. Fletcher Professor, Boston University
6th Meeting of the GLG on AMR, Bridgetown, 8 February 2023
Governments should close the funding gap for early-stage product development
Five Joint Recommendations to the GLG on R&D and Access

1. WHO should formalize a numerical target of “highly-impactful” antibacterial treatments (including innovative products as well as paediatric formulations and combinations of new and existing and antibiotics) for the next decade so that governments and philanthropic organizations, with the support of the Global AMR R&D Hub, can compare needed and expected investments to guide their long-term funding.

2. Governments should close the funding gap for early-stage product development in order to replenish the clinical pipeline with much-needed innovative and “highly-impactful” projects.

3. Governments should close the funding gap for clinical development, registration, manufacturing, post-approval trials and sustainable access in high-burden LMICs.

4. Government should implement pull incentives that bring private investors back into antibacterial R&D while ensuring equitable and sustainable access globally.

5. Provided there are adequate funding and financing mechanisms in place, pharmaceutical companies should align their R&D programs to address unmet needs defined under the WHO Priority Pathogen List, and assure equitable and sustainable access to new and existing antibiotics.
Funding early-stage R&D is urgent and indispensable

- Without a healthy early-stage development pipeline, there will be no R&D projects to develop clinically and no treatments to make accessible.

- Early-stage R&D is where the most promising but most vulnerable projects are.
  - The AMR Action Fund has struggled to find investment opportunities, with Henry Skinner saying the clinical pipeline is “much thinner” than he had originally realized (Jan 2023)
  - WHO agrees that “the clinical pipeline and recently approved antibiotics are insufficient to tackle the challenge of increasing emergence and spread of AMR.” In contrast, “[t]he preclinical pipeline is innovative and includes a large number of non-traditional approaches” (May 2022)
  - Yet, “[t]he preclinical antibacterial pipeline continues to rely on micro (< 10 employees) and small (< 50 employees) companies and academic institutions,” and the “analysis of groups with programmes in the preclinical antibacterial pipeline clearly indicates significant volatility and turnover in the R&D ecosystem” (May 2022)
6+ innovative high-impact treatments are needed per decade

<table>
<thead>
<tr>
<th>Report/strategy</th>
<th>Target (therapeutics)</th>
<th>Extrapolation for 10 years</th>
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</thead>
<tbody>
<tr>
<td>IDSA 10x20</td>
<td>10 “new systemic” over 10 years</td>
<td>10</td>
</tr>
<tr>
<td>AMR Review</td>
<td>15 “new”, of which at least 4 “breakthrough”, over a decade</td>
<td>15 (of which 4 breakthrough)</td>
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<tr>
<td>GUARD</td>
<td>One additional “high-need” per year</td>
<td>10</td>
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<tr>
<td>DRIVE-AB</td>
<td>16-20 “truly innovative” over 30 years</td>
<td>5-7</td>
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<tr>
<td>U.S. NAP 2020-2025</td>
<td>Three “new” by 2025</td>
<td>6</td>
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<tr>
<td>BARDA Strategic Plan 2022-2026</td>
<td>Three “novel” by 2026</td>
<td>6</td>
</tr>
</tbody>
</table>
### Basic Research

- **~$3 billion**

### Early-stage product development

- **~$5.6 billion**

### Advanced development and post-approval

- **~$3.3 billion**

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**Important**: These estimates do not account for the costs of regulatory submissions, post approval and access in high-burden low- and middle-income countries. Also, TB is not included.

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### 6+ innovative high-impact treatments require a pipeline

<table>
<thead>
<tr>
<th>Stage</th>
<th>Cost</th>
<th>Number of Projects</th>
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<tbody>
<tr>
<td>Basic Research</td>
<td>~$3 billion</td>
<td></td>
</tr>
<tr>
<td>Early-stage product development</td>
<td>~$5.6 billion</td>
<td>~215</td>
</tr>
<tr>
<td>Advanced development and post-approval</td>
<td>~$3.3 billion</td>
<td>~12</td>
</tr>
<tr>
<td>Total</td>
<td>~$3 billion</td>
<td>~6000</td>
</tr>
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**Preliminary results** based on probabilities of success and phase costs from best available data. Validation is underway with upstream and downstream partners, including AMRAF and GARDP.
A comparison between what is expected and what is needed

How much public and private funding can be EXPECTED for AMR R&D therapeutics in the coming 10 years

- Basic research: $2.9 billion
- Early-stage product development (from H2L to FIH): $1.8 billion
- Advanced development and post-approval in HICs: $2.6 billion

How much funding is NEEDED to obtain 6 innovative high-impact treatments in the coming 10 years

- $3 billion
- $5.6 billion
- $3.3 billion

The largest funding gap is in early-stage product development.

IMPORTANT: These estimates do not account for the costs of regulatory submissions, post approval and access in low- and middle-income countries. Also, TB is not included.

Preliminary results based on probabilities of success and phase costs from best available data. Validation is underway with upstream and downstream partners, including AMRAF and GARDP.
CARB-X: the global engine of antibacterial innovation
A **global non-profit partnership** developing antibiotics, vaccines and diagnostics to fight drug-resistant bacteria
Product developers supported since 2017
CARB-X accelerates the early-stage development of innovative products against drug-resistant bacteria

- Provides non-dilutive funding and comprehensive business, technical and scientific support to R&D projects in early-stage product development up to First-in-Human studies (product developers assume 30-40% cost-share)
- Invested more than $400M since 2017
- Created the world’s most promising discovery & early-development portfolio to address AMR, with significant progress already

1163 expressions of interest
92 projects since 2017 from 12 countries
33 active projects as of 31 Dec 2022
18 projects reached or surpassed first-in-human trials
8 with advanced development partnerships
2 on the market
CARB-X scope & focus

Three pillars that address serious bacterial threats:

• **prevent**: e.g., vaccines, live biotherapeutics, bacteriophage and antibodies

• **diagnose**: e.g., bacterial ID and Antimicrobial Susceptibility Testing

• **treat**: e.g., antibiotics and non-traditional therapeutics such as virulence modifiers, proteins, antibodies, bacteriophage

Translational research and early-clinical stages of development:

• “hit-to-lead” through a demonstration of safety in healthy-human or patient populations in clinical trials, for Tx and Pv

• feasibility through validation & verification, for Dx

**Focus** is on the greatest bacterial threats to human health, primarily:

• syndromes where AMR is attributable to greatest mortality and morbidity, caused by

• pathogens emphasized on both the WHO/CDC bacterial threats lists
**CARB-X works at scale, with a proactive portfolio strategy**

*Profile of the 92 projects since inception*

- **62** therapeutics
  - 32 projects focused on new antibiotic classes; 1 enhancement to a known class
  - 23 non-traditional projects (immune-directing, proteins, peptides, anti-virulence, engineered bacteriophage)
  - 3 therapeutics in active FIH studies

- **15** preventatives
  - 8 vaccines
  - 3 live biotherapeutics
  - 3 CRISPR-phage
  - 1 monoclonal antibody
  - 1 preventative in active FIH studies

- **15** rapid diagnostics

Detailed pipeline [https://carb-x.org/portfolio/portfolio-pipeline/](https://carb-x.org/portfolio/portfolio-pipeline/)
CARB-X targets the most deadly and burdensome threats

Global deaths attributable to (dark grey) and associated with (light grey) drug-resistant bacterial infections, by syndrome, 2019*

Source: Antimicrobial Resistance Collaborators, The Lancet, published online January 20, 2022
*: mostly targeted secondary indication
CARB-X funding comes with a contractual obligation for Stewardship & Access Plans (SAPs)

- Product developers prepare a non-confidential SAP when product enters pivotal clinical trials
  - Every CARB-X PD has agreed to the same terms
- SAP updated and published on CARB-X website when product is first approved by any of the FDA, EMA (or national authorities), MHRA, or PMDA
  - Updated following any significant market or product changes
- Obligations survive termination/expiration of CARB-X funding; follows the product to the expiration of Project IP Rights
- Wellcome Trust succeeds to CARB-X’s rights, if need be
A central and indispensable link of the R&D chain

Basic research

Early-Stage Product Development

Advanced development

Coordination via

CARB-X

Combating Antibiotic-Resistant Bacteria

(closing)

(mainly TB)

(paused)
CARB-X: Who we are

- **Non-profit**, driven by public health objectives & unmet medical need
- **Public-private partnership**, leveraging private sector expertise while funded and governed by governments and private foundations committed to global health
- **Endorsed by G7 and G20**
- **Crucial translational link of the R&D chain in between basic research and advanced development**, coordinating closely with upstream and downstream funders, including NIAID, JPIAMR, BARDA, AMR Action Fund and GARDP
- **Already working at scale (>1200 applications, >90 projects, $400m) and globally (applications from 39 countries in five continents)**, with a portfolio strategy that diversifies scientific approaches and increases the likelihood of success
- **Lean and efficient**, with 95% of funding going to product developers via non-dilutive grants and in-kind support
CARB-X: What we do

- Target the most dangerous and burdensome drug-bug-syndrome combinations based on WHO / CDC data & and the 2022 GRAM study
- Translate early-stage product development, where projects are most innovative and product developers are most vulnerable
- Accelerate products across three pillars: treatment, prevention, and diagnosis
- Support breakthrough scientific advances, including new drug classes, bacteriophages and microbiome-based approaches
- Every funding contract includes identical stewardship & access obligations
- Comprehensive scientific, regulatory and business support in addition to grants
- Portfolio Acceleration Tools which support multiple product developers, including the wider ecosystem not currently funded by CARB-X
Q&A

Website: https://carb-x.org/ | Email: mko@bu.edu | Twitter: @koutterson